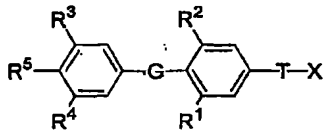
Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

Claim 1 (original): A compound of Formula I:



wherein:

G is selected from the group consisting of-O-, -S-, -S(=O)-, -S(=O)$_2$-, -CH$_2$-, -CF$_2$-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C$_1$-C$_4$ alkyl)-;

T is selected from the group consisting of -(CR$^a_2$)$_k$-, -CR^b=R^b-(CR$^a_2$)$_n$-, -(CR$^a_2$)$_n$-CR^b=CR^b-, -CR$^a_2$)-CR^b=CR^b-(CR$^a_2$)-, -O(CR$^b_2$)(CR$^a_2$)$_n$-, -S(CR$^b_2$)(CR$^a_2$)$_n$-, -N(R^c)(CR$^b_2$)(CR$^a_2$)$_n$-, -N(R^b)C(O)(CR$^a_2$)$_n$-, -(CR$^a_2$)$_n$CH(NR^{b}R^c)-, -C(O)(CR$^a_2$)$_m$-, -(CR$^a_2$)$_m$C(O)-, -(CR$^a_2$)C(O)(CR$^a_2$)$_n$-, -(CR$^a_2$)$_n$C(O)(CR$^a_2$)-, and -C(O)NH(CR$^b_2$)(CR$^a_2$)$_p$-;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C$_1$-C$_4$ alkyl, halogen, -OH, optionally substituted -O-C$_1$-C$_4$ alkyl, -OCF$_3$, optionally substituted -S-C$_1$-C$_4$ alkyl, -NR^{b}R^c, optionally substituted -C$_2$-C$_4$ alkenyl, and optionally substituted -C$_2$-C$_4$ alkynyl; with the proviso that when one R^a is

attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted -C_1-C_4 alkyl;

Each R^c is independently selected from the group consisting of hydrogen and optionally substituted -C_1-C_4 alkyl, optionally substituted -C(O)-C_1-C_4 alkyl, and -C(O)H;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted -C_1-C_4 alkyl, optionally substituted -S-C_1-C_3 alkyl, optionally substituted -C_2-C_4 alkenyl, optionally substituted -C_2-C_4 alkynyl, -CF_3, -OCF_3, optionally substituted-O-C_1-C_3 alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, -CF_3, -OCF_3, cyano, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_m$aryl, optionally substituted -$(CR^a_2)_m$cycloalkyl, optionally substituted -$(CR^a_2)_m$heterocycloalkyl, -OR^d, -SR^d, -S(=O)R^e, -$S(=O)_2R^e$, -$S(=O)_2NR^fR^g$, -C(O)NR^fR^g, -C(O)OR^h, -C(O)R^e, -N(R^bC(O)R^e, -N(R^b)C(O)NR^fR^g, -N(R^b)$S(=O)_2R^e$, -N(R^b)$S(=O)_2NR^fR^g$, and -NR^fR^g;

Each R^d is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, optionally substituted -$(CR^b_2)_n$heterocycloalkyl, and -C(O)NR^fR^g;

Each R^e is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_n$aryl, optionally substituted -$(CR^a_2)_n$cycloalkyl, and optionally substituted -$(CR^a_2)_n$heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted $(CR^b_2)_n$heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C_1-C_4 alkyl, -OR^b, oxo, cyano, -CF_3, optionally substituted phenyl, and -$C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted -$(CR^b_2)_n$heterocycloalkyl;

R^5 is selected from the group consisting of -OH, optionally substituted -OC_1-C_6 alkyl, $OC(O)R^e$, -$OC(O)OR^h$, -F, -$NHC(O)R^e$, -$NHS(=O)R^e$, -$NHS(=O)_2R^e$, -$NHC(=S)NH(R^h)$, and -$NHC(O)NH(R^h)$;

X is $P(O)YR^{11}Y'R^{11}$;

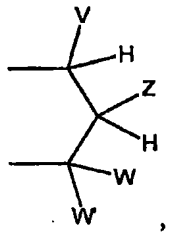
Y and Y' are each independently selected from the group consisting of -O-, and -NR^v-; when Y and Y' are -O-, R^{11} attached to -O- is independently selected from

consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z{}_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are $-NR^v-$, then R^{11} attached to $-NR^v-$ is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

when Y is -O- and Y' is NR^v, then R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycIoakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z{}_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-$ $OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^v-$ is independently selected from the group consisting of H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

or when Y and Y' are independently selected from -O- and $-NR^v-$, then together R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0–2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^zOH$, $-CHR^zOC(O)R^y$, $-CHR^zOC(S)R^y$, $-CHR^zOC(S)OR^y$, $-CHR^zOC(O)SR^y$, $-CHR^zOCO_2R^y$, $-OR^z$, $-SR^z$, $-CHR^zN_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH{=}CR^z{}_2)OH$, $-CH(C{\equiv}CR^z)OH$, $-R^z$, $-NR^z{}_2$, $-OCOR^y$, $-OCO_2R^y$, $-SCOR^y$, $-SCO_2R^y$, $-NHCOR^z$, $-NHCO_2R^y$, $-CH_2$NHaryl, $-(CH_2)_q-OR^z$, and $-(CH_2)_q-SR^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^y is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

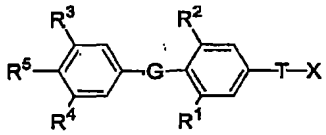
a) when G is -O-, T is $-CH_2-$, R^1 and R^2 are each bromo, R^3 is *iso*-propyl, R^4 is hydrogen, and R^5 is –OH, then X is not $P(O)(OH)_2$ or $P(O)(OCH_2CH_3)_2$;

b) V, Z, W, W' are not all -H; and

c) when Z is $-R^z$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

Claim 2 (original): A compound of Formula I:



wherein:

G is selected from the group consisting of-O-, -S-, -S(=O)-, $-S(=O)_2-$, $-CH_2-$, $-CF_2-$, -CHF-, -C(O)-, -CH(OH)-, -NH-, and $-N(C_1-C_4$ alkyl)-;

T is selected from the group consisting of $-(CR^a{}_2)_k-$, $-CR^b=R^b-(CR^a{}_2)_n-$, $-(CR^a{}_2)_n-CR^b=CR^b-$, $-CR^a{}_2)-CR^b=CR^b-(CR^a{}_2)-$, $-O(CR^b{}_2)(CR^a{}_2)_n-$, $-S(CR^b{}_2)(CR^a{}_2)_n-$, $-N(R^c)(CR^b{}_2)(CR^a{}_2)_n-$, $-N(R^b)C(O)(CR^a{}_2)_n-$, $-(CR^a{}_2)_nCH(NR^bR^c)-$, $-C(O)(CR^a{}_2)_m-$, $-(CR^a{}_2)_mC(O)-$, $-(CR^a{}_2)C(O)(CR^a{}_2)_n-$, $-(CR^a{}_2)_nC(O)(CR^a{}_2)-$, and $-C(O)NH(CR^b{}_2)(CR^a{}_2)_p-$;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted $-C_1-C_4$ alkyl, halogen, -OH, optionally substituted $-O-C_1-C_4$ alkyl, $-OCF_3$, optionally substituted $-S-C_1-C_4$ alkyl, $-NR^bR^c$, optionally substituted $-C_2-C_4$ alkenyl, and optionally substituted $-C_2-C_4$ alkynyl; with the proviso that when

one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted -C_1-C_4 alkyl;

Each R^c is independently selected from the group consisting of hydrogen and optionally substituted -C_1-C_4 alkyl, optionally substituted -C(O)-C_1-C_4 alkyl, and -C(O)H;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted -C_1-C_4 alkyl, optionally substituted -S-C_1-C_3 alkyl, optionally substituted -C_2-C_4 alkenyl, optionally substituted -C_2-C_4 alkynyl, -CF_3, -OCF_3, optionally substituted-O-C_1-C_3 alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, -CF_3, -OCF_3, cyano, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_m$aryl, optionally substituted -$(CR^a_2)_m$cycloalkyl, optionally substituted -$(CR^a_2)_m$heterocycloalkyl, -OR^d, -SR^d, -S(=O)R^e, -$S(=O)_2R^e$, -$S(=O)_2NR^fR^g$, -C(O)NR^fR^g, -C(O)OR^h, -C(O)R^e, -N(R^b)C(O)R^e, -N(R^b)C(O)NR^fR^g, -N(R^b)$S(=O)_2R^e$, -N(R^b)$S(=O)_2NR^fR^g$, and -NR^fR^g;

Each R^d is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, optionally substituted -$(CR^b_2)_n$heterocycloalkyl, and -C(O)NR^fR^g;

Each R^e is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_n$aryl, optionally substituted -$(CR^a_2)_n$cycloalkyl, and optionally substituted -$(CR^a_2)_n$heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted $(CR^b_2)_n$heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C_1-C_4 alkyl, -OR^b, oxo, cyano, -CF_3, optionally substituted phenyl, and -$C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted -$(CR^b_2)_n$heterocycloalkyl;

R^5 is selected from the group consisting of -OH, optionally substituted -OC_1-C_6 alkyl, $OC(O)R^e$, -$OC(O)OR^h$, -F, -$NHC(O)R^e$, -$NHS(=O)R^e$, -$NHS(=O)_2R^e$, -$NHC(=S)NH(R^h)$, and -$NHC(O)NH(R^h)$;

X is $P(O)YR^{11}Y'R^{11}$;

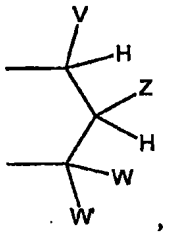
Y and Y' are each independently selected from the group consisting of -O-, and -NR^v-; when Y and Y' are -O-, R^{11} attached to -O- is independently selected from

consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z{}_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are $-NR^v-$, then R^{11} attached to $-NR^v-$ is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

when Y is -O- and Y' is NR^v, then R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z{}_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^v-$ is independently selected from the group consisting of H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR$ y, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

or when Y and Y' are independently selected from -O- and $-NR^v-$, then together R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0–2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^zOH$, $-CHR^zOC(O)R^y$, $-CHR^zOC(S)R^y$, $-CHR^zOC(S)OR^y$, $-CHR^zOC(O)SR^y$, $-CHR^zOCO_2R^y$, $-OR^z$, $-SR^z$, $-CHR^zN_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^z{}_2)OH$, $-CH(C\equiv CR^z)OH$, $-R^z$, $-NR^z{}_2$, $-OCOR^y$, $-OCO_2R^y$, $-SCOR^y$, $-SCO_2R^y$, $-NHCOR^z$, $-NHCO_2R^y$, $-CH_2$NHaryl, $-(CH_2)_q-OR^z$, and $-(CH_2)_q-SR^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

a) when G is -O-, T is $-(CH_2)_{0-4}-$, R^1 and R^2 are independently halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R^3 is alkyl of 1 to 4 carbons or

cycloalkyl of 3 to 7 carbons, R^4 is hydrogen, and R^5 is -OH, then X is not $-P(O)(OH)_2$ or $-P(O)(O\text{-lower alkyl})_2$;

b) when G is -O-, R^5 is $NHC(O)R^e$, $NHS(=O)_{1-2}R^e$, $-NHC(S)NH(R^h)$, or $-NHC(O)NH(R^h)$, T is $-(CH_2)_m-$, -CH=CH-, $-O(CH_2)_{1-2}-$, or $-NH(CH_2)_{1-2}-$, then X is not $-P(O)(OH)_2$ or $-P(O)(OH)NH_2$;

c) V, Z, W, W' are not all -H; and

d) when Z is $-R^z$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

Claims 3-82 (canceled)

Claim 83 (original): A method of preventing or treating a metabolic disease comprising administering to an animal a pharmaceutically effective amount of a phosphonic acid-containing compound, a pharmaceutically acceptable salt thereof, or prodrugs thereof or pharmaceutically acceptable salts of said prodrugs, wherein said phosphonic acid containing compound binds to a thyroid receptor.

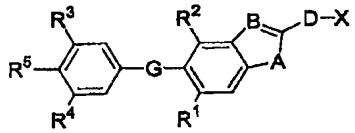
Claims 84-99 (canceled)

Claim 100 (original): A method of activating a thyroid receptor in an animal by administering a phosphonic acid-containing-compound wherein said activation results in

the 50% or greater increase in the mRNA expression of a gene selected from the group consisting of LDL receptor, ACC, FAS, spot-14, CPT-1, CYP7A, apo AI, and mGPDH.

Claims 101-116 (canceled)

Claim 117 (original): A compound of Formula II:



wherein:

A is selected from the group consisting of -NR^i-, -O-, and -S-;

B is selected from the group consisting of—CR^b-, and -N-;

R^i is selected from the group consisting of hydrogen, -$C(O)C_1$-C_4 alkyl, -C_1-C_4 alkyl, and -C_1-C_4-aryl;

R^b is selected from the group consisting of hydrogen and optionally substituted -C_1-C_4 alkyl;

G is selected from the group consisting of -O-, -S-, -S(=O)-, -$S(=O)_2$-, -CH_2-, -CF_2-, -CHF-, -C(O)-, -CH(OH)-, NH-, and -N(C_1-C_4 alkyl)-;

D is selected from the group consisting of a bond, -(CR^a_2) -, and -C(O)-;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C_1-C_4 alkyl, halogen, -OH, optionally substituted -O-C_1-C_4 alkyl, -OCF_3, optionally substituted -S-C_1-C_4 alkyl, -NR^bR^c, optionally substituted -C_2-C_4 alkenyl, and optionally substituted -C_2-C_4 alkynyl; with the proviso that when one R^a is

attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted -C_1-C_4 alkyl, optionally substituted -S-C_1-C_3 alkyl, optionally substituted -C_2-C_4 alkenyl, optionally substituted -C_2-C_4 alkynyl, -CF_3, -OCF_3, optionally substituted-O-C_1-C_3 alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, -CF_3, -OCF_3, cyano, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_m$aryl, optionally substituted -$(CR^a_2)_m$cycloalkyl, optionally substituted -$(CR^a_2)_m$heterocycloalkyl, -OR^d, -SR^d, -S(=O)R^e, -S(=O)$_2R^e$, -S(=O)$_2NR^fR^g$, -C(O)NR^fR^g, -C(O)OR^h, -C(O)R^e, -N(R^b)C(O)R^e, -N(R^b)C(O)NR^fR^g, -N(R^b)S(=O)$_2R^e$, -N(R^b)S(=O)$_2NR^fR^g$, and -NR^fR^g;

Each R^d is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, optionally substituted -$(CR^b_2)_n$heterocycloalkyl, and -C(O)NR^fR^g;

Each R^e is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_n$aryl, optionally substituted -$(CR^a_2)_n$cycloalkyl, and optionally substituted -$(CR^a_2)_n$heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally

substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted $(CR^b_2)_n$heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C_1-C_4 alkyl, -OR^b, oxo, cyano, -CF_3, optionally substituted phenyl, and -$C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted -$(CR^b_2)_n$heterocycloalkyl;

R^5 is selected from the group consisting of -OH, optionally substituted -OC_1-C_6 alkyl, $OC(O)R^e$, -$OC(O)OR^h$, -F, -$NHC(O)R^e$, -$NHS(=O)R^e$, -$NHS(=O)_2R^e$, -$NHC(=S)NH(R^h)$, and -$NHC(O)NH(R^h)$;

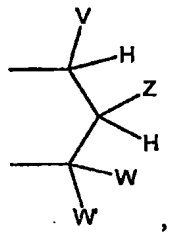
X is $P(O)YR^{11}Y'R^{11}$;

Y and Y' are each independently selected from the group consisting of -O-, and -NR^v-; when Y and Y' are -O-, R^{11} attached to -O- is independently selected from consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -$C(R^z)_2OC(O)NR^z_2$, -NR^z-C(O)-R^y, -$C(R^z)_2$-$OC(O)^y$, -$C(R^z)_2$-O-$C(O)OR^y$, -$C(R^z)_2OC(O)SR^y$, -alkyl-S-$C(O)R^y$, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are $-NR^v-$, then R^{11} attached to $-NR^v-$ is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

when Y is -O- and Y' is NR^v, then R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-$C(O)R^y$, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^v-$ is independently selected from the group consisting of H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

or when Y and Y' are independently selected from -O- and $-NR^v-$, then together R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,

substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0–2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^zOH$, $-CHR^zOC(O)R^y$, $-CHR^zOC(S)R^y$, $-CHR^zOC(S)OR^y$, $-CHR^zOC(O)SR^y$, $-CHR^zOCO_2R^y$, $-OR^z$, $-SR^z$, $-CHR^zN_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^z_2)OH$, $-CH(C\equiv CR^z)OH$, $-R^z$, $-NR^z_2$, $-OCOR^y$, $-OCO_2R^y$, $-SCOR^y$, $-SCO_2R^y$, $-NHCOR^z$, $-NHCO_2R^y$, $-CH_2$NHaryl, $-(CH_2)_q-OR^z$, and $-(CH_2)_q-SR^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

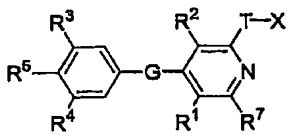
a) V, Z, W, W' are not all -H; and

b) when Z is $-R^z$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

Claims 118-138 (canceled)

Claim 139 (original): A compound of Formula III:



wherein:

G is selected from the group consisting of-O-, -S-, -S(=O)-, -S(=O)$_2$-, -CH$_2$-, -CF$_2$-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C$_1$-C$_4$ alkyl)-;

T is selected from the group consisting of -(CR$^a_2$)$_k$-, -CR^b=R^b-(CR$^a_2$)$_n$-, -(CR$^a_2$)$_n$-CR^b=CR^b-, -(CR$^a_2$)-CR^b=CR^b-(CR$^a_2$)-, -O(CR$^b_2$)(CR$^a_2$)$_n$-, -S(CR$^b_2$)(CR$^a_2$)$_n$-, -N(R^c)(CR$^b_2$)(CR$^a_2$)$_n$-, -N(R^b)C(O)(CR$^a_2$)$_n$-, -(CR$^a_2$)$_n$CH(NR^{b}R^c)-, -C(O)(CR$^a_2$)$_m$-, -(CR$^a_2$)$_m$C(O)-, -(CR$^a_2$)C(O)(CR$^a_2$)$_n$-, -(CR$^a_2$)$_n$C(O)(CR$^a_2$)-, and -C(O)NH(CR$^b_2$)(CR$^a_2$)$_p$-;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C$_1$-C$_4$ alkyl, halogen, -OH, optionally substituted -O-C$_1$-C$_4$ alkyl, -OCF$_3$, optionally substituted -S-C$_1$-C$_4$ alkyl, -NR^{b}R^c, optionally substituted -C$_2$-C$_4$ alkenyl, and optionally substituted -C$_2$-C$_4$ alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted -C$_1$-C$_4$ alkyl;

Each R^c is independently selected from the group consisting of hydrogen and optionally substituted -C_1-C_4 alkyl, optionally substituted -C(O)-C_1-C_4 alkyl, and -C(O)H;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted -C_1-C_4 alkyl, optionally substituted -S-C_1-C_3 alkyl, optionally substituted -C_2-C_4 alkenyl, optionally substituted -C_2-C_4 alkynyl, -CF_3, -OCF_3, optionally substituted-O-C_1-C_3 alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, -CF_3, -OCF_3, cyano, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_m$aryl, optionally substituted -$(CR^a_2)_m$cycloalkyl, optionally substituted -$(CR^a_2)_m$heterocycloalkyl, -OR^d, -SR^d, -S(=O)R^e, -$S(=O)_2R^e$, -$S(=O)_2NR^fR^g$, -C(O)NR^fR^g, -C(O)OR^h, -C(O)R^e, -$N(R^b)C(O)R^e$, -$N(R^b)C(O)NR^fR^g$, -$N(R^b)S(=O)_2R^e$, -$N(R^b)S(=O)_2NR^fR^g$, and -NR^fR^g;

Each R^d is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, optionally substituted -$(CR^b_2)_n$heterocycloalkyl, and -C(O)NR^fR^g;

Each R^e is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_n$aryl, optionally substituted -$(CR^a_2)_n$cycloalkyl, and optionally substituted -$(CR^a_2)_n$heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted $(CR^b_2)_n$heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C_1-C_4 alkyl, -OR^b, oxo, cyano, -CF_3, optionally substituted phenyl, and -$C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted -$(CR^b_2)_n$heterocycloalkyl;

R^5 is selected from the group consisting of -OH, optionally substituted -OC_1-C_6 alkyl, $OC(O)R^e$, -$OC(O)OR^h$, -F, -$NHC(O)R^e$, -$NHS(=O)R^e$, -$NHS(=O)_2R^e$, -$NHC(=S)NH(R^h)$, and -$NHC(O)NH(R^h)$;

R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C_1-C_4 alkyl, -SH and -S-C_1-C_4 alkyl;

X is $P(O)YR^{11}Y'R^{11}$;

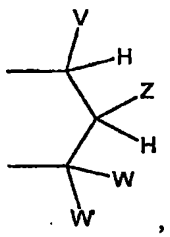
Y and Y' are each independently selected from the group consisting of -O-, and -NR^v-; when Y and Y' are -O-, R^{11} attached to -O- is independently selected from consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycloakyl wherein the cyclic moiety

contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are $-NR^v-$, then R^{11} attached to $-NR^v-$ is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

when Y is -O- and Y' is NR^v, then R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^v-$ is independently selected from the group consisting of H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

or when Y and Y' are independently selected from -O- and $-NR^v-$, then together R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the group:



,

wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0–2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^zOH$, $-CHR^zOC(O)R^y$, $-CHR^zOC(S)R^y$, $-CHR^zOC(S)OR^y$, $-CHR^zOC(O)SR^y$, $-CHR^zOCO_2R^y$, $-OR^z$, $-SR^z$, $-CHR^zN_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^z{}_2)OH$, $-CH(C\equiv CR^z)OH$, $-R^z$, $-NR^z{}_2$, $-OCOR^y$, $-OCO_2R^y$, $-SCOR^y$, $-SCO_2R^y$, $-NHCOR^z$, $-NHCO_2R^y$, $-CH_2$NHaryl, $-(CH_2)_q-OR^z$, and $-(CH_2)_q-SR^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

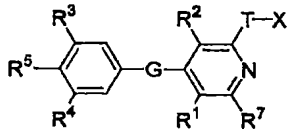
a) when G is -O-, T is $-NH-CH_2-$, R^1 and R^2 are each chloro, R^3 is *iso*-propyl, R^4 is hydrogen, R^7 is fluoro, and R^5 is –OH, then X is not $P(O)(OH)_2$, $P(O)(OH)(OCH_3)$ or $P(O)(OCH_3)_2$;

b) V, Z, W, W' are not all -H; and

c) when Z is-R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

Claim 140 (original): A compound of Formula III:



wherein:

G is selected from the group consisting of-O-, -S-, -S(=O)-, -S(=O)$_2$-, -CH_2-, -CF_2-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C_1-C_4 alkyl)-;

T is selected from the group consisting of -$(CR^a{}_2)_k$-, -CR^b=R^b-$(CR^a{}_2)_n$-, -$(CR^a{}_2)_n$-CR^b=CR^b-, -$(CR^a{}_2)$-CR^b=CR^b-$(CR^a{}_2)$-, -O$(CR^b{}_2)(CR^a{}_2)_n$-, -S$(CR^b{}_2)(CR^a{}_2)_n$-, -N$(R^c)(CR^b{}_2)(CR^a{}_2)_n$-, -N$(R^b)$C(O)$(CR^a{}_2)_n$-, -$(CR^a{}_2)_nCH(NR^bR^c)$-, -C(O)$(CR^a{}_2)_m$-, -$(CR^a{}_2)_m$C(O)-, -$(CR^a{}_2)$C(O)$(CR^a{}_2)_n$-, -$(CR^a{}_2)_n$C(O)$(CR^a{}_2)$-, and -C(O)NH$(CR^b{}_2)(CR^a{}_2)_p$-;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C_1-C_4 alkyl, halogen, -OH, optionally substituted -O-C_1-C_4 alkyl, -OCF_3, optionally substituted -S-C_1-C_4 alkyl, -NR^bR^c, optionally substituted -C_2-C_4 alkenyl, and optionally substituted -C_2-C_4 alkynyl; with the proviso that when one R^a is

attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted -C_1-C_4 alkyl;

Each R^c is independently selected from the group consisting of hydrogen and optionally substituted -C_1-C_4 alkyl, optionally substituted -C(O)-C_1-C_4 alkyl, and -C(O)H;

R^1 and R^2 are each independently selected from the group consisting of halogen, optionally substituted -C_1-C_4 alkyl, optionally substituted -S-C_1-C_3 alkyl, optionally substituted -C_2-C_4 alkenyl, optionally substituted -C_2-C_4 alkynyl, -CF_3, -OCF_3, optionally substituted-O-C_1-C_3 alkyl, and cyano;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, -CF_3, -OCF_3, cyano, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_m$aryl, optionally substituted -$(CR^a_2)_m$cycloalkyl, optionally substituted -$(CR^a_2)_m$heterocycloalkyl, -OR^d, -SR^d, -S(=O)R^e, -$S(=O)_2R^e$, -$S(=O)_2NR^fR^g$, -C(O)NR^fR^g, -C(O)OR^h, -C(O)R^e, -$N(R^b)C(O)R^e$, -$N(R^b)C(O)NR^fR^g$, -$N(R^b)S(=O)_2R^e$, -$N(R^b)S(=O)_2NR^fR^g$, and -NR^fR^g;

Each R^d is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, optionally substituted -$(CR^b_2)_n$heterocycloalkyl, and -C(O)NR^fR^g;

Each R^e is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_n$aryl, optionally substituted -$(CR^a_2)_n$cycloalkyl, and optionally substituted -$(CR^a_2)_n$heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted $(CR^b_2)_n$heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C_1-C_4 alkyl, -OR^b, oxo, cyano, -CF_3, optionally substituted phenyl, and -$C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted -$(CR^b_2)_n$heterocycloalkyl;

R^5 is selected from the group consisting of -OH, optionally substituted -OC_1-C_6 alkyl, $OC(O)R^e$, -$OC(O)OR^h$, -F, -$NHC(O)R^e$, -$NHS(=O)R^e$, -$NHS(=O)_2R^e$, -$NHC(=S)NH(R^h)$, and -$NHC(O)NH(R^h)$;

R^7 is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C_1-C_4 alkyl, -SH and -S-C_1-C_4 alkyl;

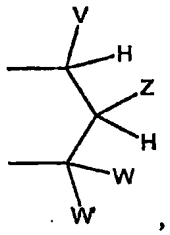
X is $P(O)YR^{11}Y'R^{11}$;

Y and Y' are each independently selected from the group consisting of -O-, and $-NR^v-$; when Y and Y' are -O-, R^{11} attached to -O- is independently selected from consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are $-NR^v-$, then R^{11} attached to $-NR^v-$ is independently selected from the group consisting of -H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

when Y is -O- and Y' is NR^v, then R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycIoakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^v-$ is independently selected from the group consisting of H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

or when Y and Y' are independently selected from -O- and $-NR^v-$, then together R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0–2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^zOH$, $-CHR^zOC(O)R^y$, $-CHR^zOC(S)R^y$, $-CHR^zOC(S)OR^y$, $-CHR^zOC(O)SR^y$, $-CHR^zOCO_2R^y$, $-OR^z$, $-SR^z$, $-CHR^zN_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^z{}_2)OH$, $-CH(C\equiv CR^z)OH$, $-R^z$, $-NR^z{}_2$, $-OCOR^y$, $-OCO_2R^y$, $-SCOR^y$, $-SCO_2R^y$, $-NHCOR^z$, $-NHCO_2R^y$, $-CH_2$NHaryl, $-(CH_2)_q-OR^z$, and $-(CH_2)_q-SR^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

a) when G is selected from the group consisting of -O-, -S-, -S(=O)-, $-S(=O)_2-$, $-CH_2-$, -C(O)- and NR^b-; T is –A-B- where A is selected from the group consisting of $-NR^b-$, -O-, $-CH_2-$ and –S- and B is selected from the group consisting of a

bond and substituted or unsubstituted C_1-C_3 alkyl; R^3 is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C_3-C_7 cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R^4 is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; R^1 and R^2 are each independently selected from the group consisting of halogen, substituted or unsubstituted C_1-C_4 alkyl, and substituted or unsubstituted C_3-C_5 cycloalkyl; R^7 is selected selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C_1-C_4 alkyl, -SH and -S-C_1-C_4 alkyl; and R^5 is selected from the group consisting of hydroxyl, optionally substituted -OC_1-C_6 alkyl, and -OC(O)R^e; then X is not -P(O)$(OH)_2$;

b) V, Z, W, W' are not all -H; and

c) when Z is -R^z, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

Claims 141-226 (canceled)

Claim 227 (original): A phosphonic acid containing thyromimetic compound of Formula X:

(Ar^1)-G-(Ar^2)-T-X

wherein:

Ar^1 and Ar^2 are aryl groups;

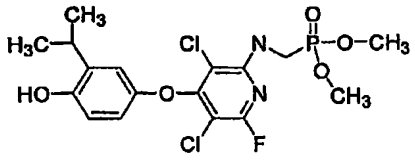
G is an atom or group of atoms that links Ar^1 and Ar^2 through a single C, S, O, or N atom;

T is an atom or group of atoms linking Ar^2 to X through 1-4 contiguous atoms or is absent;

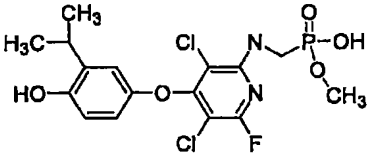
X is a —$P(O)(OH)_2$ or prodrug thereof;

wherein (Ar^1)-G-(Ar^2)-T-$P(O)(OH)_2$ has a Ki of $\leq$ 150 nM relative to T3; with the provisos that said -$P(O)(OH)_2$ containing thryomimetic compound is not:

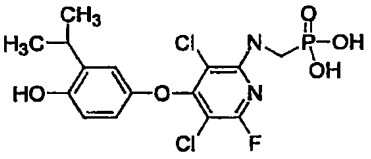
a)



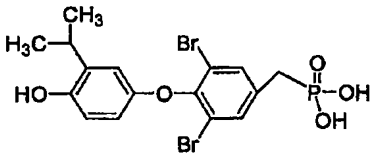
b)



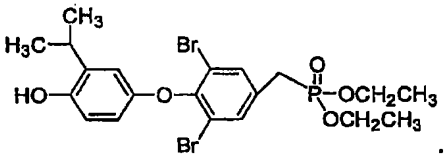
c)



d)



e)



Claim 228 (original): A method of improving liver versus heart selectivity of a thyromimetic compound of Formula Y:

(Ar^1)-G-(Ar^2)-T-E

wherein:

Ar^1 and Ar^2 are aryl groups;

G is an atom or group of atoms that links Ar^1 and Ar^2 through a single C, S, O, or N atom;

T is an atom or group of atoms linking Ar^2 to E through 1-4 contiguous atoms or is absent;

E is selected from the group consisting of a functional group or moiety with a pKa $\leq$ 7.4, a carboxylic acid moiety or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a TRα or TRβ, comprising the step of replacing E with a $-P(O)(OH)_2$ or prodrug thereof.

Claim 229 (original): A method of increasing the therapeutic index of a thyromimetic compound of Formula Y:

(Ar^1)-G-(Ar^2)-T-E

wherein:

Ar^1 and Ar^2 are aryl groups;

G is an atom or group of atoms that links Ar^1 and Ar^2 through a single C, S, O, or N atom;

T is an atom or group of atoms linking Ar^2 to E through 1-4 atoms or is absent;

E is selected from the group consisting of a functional group or moiety with a pKa $\leq$ 7.4, a carboxylic acid moiety or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a TRα or TRβ, comprising the step of

replacing E with a $-P(O)(OH)_2$ or prodrug thereof.

Claim 230 (original): A method of designing a thyromimetic compound with improved liver versus heart selectivity comprising the steps of:

obtaining a molecular formula for a thyromimetic of Formula Y:

(Ar^1)-G-(Ar^2)-T-E

wherein:

Ar^1 and A^2 are aryl groups;

G is an atom or group of atoms that links Ar^1 and Ar^2 through a single C, S, O, or N atom;

T is an atom or group of atoms linking Ar^2 to E through 1-4 contiguous atoms or is absent;

E is selected from the group consisting of a functional group or moiety with a pKa $\leq$ 7.4, a carboxylic acid moiety, or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a TRα or TRβ; comprising the step of replacing E with a $-P(O)(OH)_2$ or prodrug thereof; and synthesizing a compound of Formula X wherein X is $P(O)(OH)_2$ acid or prodrug thereof.

Claim 231 (original): A method of designing a thyromimetic compound with an improved therapeutic index comprising the steps of:

obtaining a molecular formula for a thyromimetic of Formula Y:

(Ar^1)-G-(Ar^2)-T-E

wherein:

Ar^1 and Ar^2 are aryl groups;

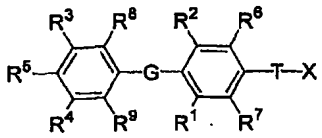
G is an atom or group of atoms that links Ar^1 and Ar^2 through a single C, S, O, or N atom;

T is an atom or group of atoms linking Ar^2 to E through 1-4 atoms or is absent;

E is selected from the group consisting of a functional group or moiety with a pKa $\leq$ 7.4, a carboxylic acid moiety, or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a TRα or TRβ; comprising the step of

replacing E with a $-P(O)(OH)_2$ or prodrug thereof; and synthesizing a compound of Formula X wherein X is $P(O)(OH)_2$ acid or prodrug thereof.

Claim 232 (original): A compound of Formula VIII:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, $-S(=O)_2-$, -Se-, $-CH_2-$, $-CF_2-$, -CHF-, -C(O)-, -CH(OH)-, -CH(C_1-C_4 alkyl)-, -CH(C_1-C_4 alkoxy)-, $-C(=CH_2)-$,-NH-, and -N(C_1-C_4 alkyl)-;

T is selected from the group consisting of $-(CR^a_2)_k-$, $-CR^b=CR^b-(CR^a_2)_n-$, $-(CR^a_2)_n-CR^b=CR^b-$, $-(CR^a_2)-CR^b=CR^b-(CR^a_2)-$, $-O(CR^b_2)(CR^a_2)_n-$, $-S(CR^b_2)(CR^a_2)_n-$, $N(R^c)(CR^b_2)(CR^a_2)_n-$, $N(R^b)C(O)(CR^a_2)_n-$, $-(CR^a_2)_nCH(NR^bR^c)-$, $-C(O)(CR^a_2)_m-$, $-(CR^a_2)_mC(O)-$, $-(CR^a_2)C(O)(CR^a_2)_n$, $-(CR^a_2)_nC(O)(CR^a_2)-$, and $-C(O)NH(CR^b_2)(CR^a_2)_p-$;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

Each R^a is independently selected from the group consisting of hydrogen, optionally substituted -C_1-C_4 alkyl, halogen, -OH, optionally substituted -O-C_1-C_4 alkyl, -OCF_3, optionally substituted -S-C_1-C_4 alkyl, -NR^bR^c, optionally substituted -C_2-C_4 alkenyl, and optionally substituted -C_2-C_4 alkynyl; with the proviso that when one R^a is attached to C through an O, S, or N atom, then the other R^a attached to the same C is a hydrogen, or attached via a carbon atom;

Each R^b is independently selected from the group consisting of hydrogen and optionally substituted -C_1-C_4 alkyl;

Each R^c is independently selected from the group consisting of hydrogen and optionally substituted -C_1-C_4 alkyl, optionally substituted -C(O)-C_1-C_4 alkyl, and -C(O)H;

R^1, R^2, R^6, R^7, R^8, and R^9 are each independently selected from the group consisting of hydrogen, halogen, optionally substituted -C_1-C_4 alkyl, optionally substituted -S-C_1-C_3 alkyl, optionally substituted -C_2-C_4 alkenyl, optionally substituted -C_2-C_4 alkynyl, -CF_3, -OCF_3, optionally substituted-O-C_1-C_3 alkyl, and cyano; with the proviso that at least one of R^1 and R^2 is not hydrogen;

or R^6 and T are taken together along with the carbons they are attached to form a ring of 5 to 6 atoms including 0 to 2 heteroatoms independently selected from —NR^i-, -O-, and –S-, with the proviso that when there are 2 heteroatoms in the ring and both heteroatoms are different than nitrogen then both heteroatoms have to be separated by at least one carbon atom; and X is attached to this ring by a direct bond to a ring carbon, or by –(CR^a_2)- or –C(O)- bonded to a ring carbon or a ring nitrogen;

R^i is selected from the group consisting of hydrogen, -C(O)C_1-C_4 alkyl, -C_1-C_4 alkyl, and -C_1-C_4-aryl;

R^3 and R^4 are each independently selected from the group consisting of hydrogen, halogen, -CF_3, -OCF_3, cyano, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_m$aryl, optionally substituted -$(CR^a_2)_m$cycloalkyl, optionally substituted -$(CR^a_2)_m$heterocycloalkyl, -OR^d, -SR^d, -S(=O)R^e, -$S(=O)_2R^e$, -$S(=O)_2NR^fR^g$, -C(O)NR^fR^g, -C(O)OR^h, -C(O)R^e, -$N(R^b)C(O)R^e$, -$N(R^b)C(O)NR^fR^g$, -$N(R^b)S(=O)_2R^e$, -$N(R^b)S(=O)_2NR^fR^g$, and -NR^fR^g;

Each R^d is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, optionally substituted -$(CR^b_2)_n$heterocycloalkyl, and -C(O)NR^fR^g;

Each R^e is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^a_2)_n$aryl, optionally substituted -$(CR^a_2)_n$cycloalkyl, and optionally substituted -$(CR^a_2)_n$heterocycloalkyl;

R^f and R^g are each independently selected from the group consisting of hydrogen, optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted $(CR^b_2)_n$heterocycloalkyl, or R^f and R^g may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR^c, and S, wherein said optionally

substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C_1-C_4 alkyl, -OR^b, oxo, cyano, -CF_3, optionally substituted phenyl, and -$C(O)OR^h$;

Each R^h is selected from the group consisting of optionally substituted -C_1-C_{12} alkyl, optionally substituted -C_2-C_{12} alkenyl, optionally substituted -C_2-C_{12} alkynyl, optionally substituted -$(CR^b_2)_n$aryl, optionally substituted -$(CR^b_2)_n$cycloalkyl, and optionally substituted -$(CR^b_2)_n$heterocycloalkyl;

R^5 is selected from the group consisting of -OH, optionally substituted -OC_1-C_6 alkyl, $OC(O)R^e$, -$OC(O)OR^h$, -F, -$NHC(O)R^e$, -$NHS(=O)R^e$, -$NHS(=O)_2R^e$, -$NHC(=S)NH(R^h)$, and -$NHC(O)NH(R^h)$;

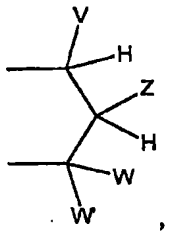
X is $P(O)YR^{11}Y'R^{11}$;

Y and Y' are each independently selected from the group consisting of -O-, and -NR^v-; when Y and Y' are -O-, R^{11} attached to -O- is independently selected from consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -$C(R^z)_2OC(O)NR^z_2$, -NR^z-C(O)-R^y, -$C(R^z)_2$-$OC(O)^y$, -$C(R^z)_2$-O-$C(O)OR^y$, -$C(R^z)_2OC(O)SR^y$, -alkyl-S-$C(O)R^y$, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are -NR^v-, then R^{11} attached to -NR^v- is independently selected from the group consisting of -H, -$[C(R^z)_2]_q$-$COOR^y$, -$C(R^x)_2COOR^y$, -$[C(R^z)_2]_q$-$C(O)SR^y$, and -cycloalkylene-$COOR^y$;

when Y is -O- and Y' is NR^v, then R^{11} attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH_2-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, $-C(R^z)_2OC(O)NR^z_2$, $-NR^z-C(O)-R^y$, $-C(R^z)_2-$ $OC(O)R^y$, $-C(R^z)_2-O-C(O)OR^y$, $-C(R^z)_2OC(O)SR^y$, -alkyl-S-C(O)R^y, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R^{11} attached to $-NR^v-$ is independently selected from the group consisting of H, $-[C(R^z)_2]_q-COOR^y$, $-C(R^x)_2COOR^y$, $-[C(R^z)_2]_q-C(O)SR^y$, and -cycloalkylene-$COOR^y$;

or when Y and Y' are independently selected from -O- and $-NR^v-$, then together R^{11} and R^{11} are -alkyl-S-S-alkyl- to form a cyclic group, or together R^{11} and R^{11} are the group:



,

wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0–1 atoms are heteroatoms and the remaining

atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0–2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^zOH$, $-CHR^zOC(O)R^y$, $-CHR^zOC(S)R^y$, $-CHR^zOC(S)OR^y$, $-CHR^zOC(O)SR^y$, $-CHR^zOCO_2R^y$, $-OR^z$, $-SR^z$, $-CHR^zN_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH{=}CR^z{}_2)OH$, $-CH(C{\equiv}CR^z)OH$, $-R^z$, $-NR^z{}_2$, $-OCOR^y$, $-OCO_2R^y$, $-SCOR^y$, $-SCO_2R^y$, $-NHCOR^z$, $-NHCO_2R^y$, $-CH_2$NHaryl, $-(CH_2)_q-OR^z$, and $-(CH_2)_q-SR^z$;

q is an integer 2 or 3;

Each R^z is selected from the group consisting of R^y and -H;

Each R^y is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R^x is independently selected from the group consisting of -H, and alkyl, or together R^x and R^x form a cyclic alkyl group;

Each R^v is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

a) when G is -O-, T is $-CH_2-$, R^1 and R^2 are each bromo, R^3 is *iso*-propyl, R^4 is hydrogen, and R^5 is –OH, then X is not $P(O)(OH)_2$ or $P(O)(OCH_2CH_3)_2$;

b) V, Z, W, W' are not all -H; and

c) when Z is $-R^z$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

d) when G is -O-, T is $-(CH_2)_{0-4}-$, R^1 and R^2 are independently halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R^3 is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, R^4 is hydrogen, and R^5 is -OH, then X is not $-P(O)(OH)_2$ or $-P(O)(O \text{ lower alkyl})_2$; and

e) when G is -O-, R^5 is $-NHC(O)R^e$, $-NHS(=O)_{1-2}R^e$, $-NHC(S)NH(R^b)$, or $-NHC(O)NH(R^h)$, T is $-(CH_2)_{m-}$, -CH=CH-, $-O(CH_2)_{1-2}-$, or $-NH(CH_2)_{1-2}-$, then X is not $-P(O)(OH)_2$ or $-P(O)(OH)NH_2$;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

Claim 233 (original): A method of increasing the liver specificity of a T3 mimetic having a carboxylic acid moiety comprising the preparation of a compound that is an analog of said T3 mimetic wherein said carboxylic acid moiety is replaced by $P(O)(OH)_2$ and prodrugs thereof.

Claim 234 (original): A method of selecting a T3 mimetic having enhanced liver specificity comprising the steps of:

a) measuring the liver specificity of a T3 mimetic having a carboxylic acid moiety;

b) measuring the liver specificity of a compound that is an analog of said T3 mimetic having a carboxylic acid moiety wherein the carboxylic acid moiety is replaced by a P(O)(OH)2 or prodrug thereof;

c) comparing the liver specificities of steps a) and b).

Claim 235 (original): A method of screening T3 mimetics comprising the steps of:

a) measuring a biological effect of T3 mimetic having a carboxylic acid moiety wherein said biological effect is selected from the group consisting of the Ki relative to T3, effects on blood glucose level, effects on serum cholesterol level, effects on fat in the liver, liver specificity, and therapeutic index;

b) measuring the same biological effect measured in a) of a T3 mimetic having a phosphonic acid or prodrug moiety thereof; and

c) comparing the results in steps a) and b);

d) selecting the T3 mimetic of step b) for further scientific evaluation.

Claims 236-238 (canceled)

Claim 239 (new): The method of claim 83 wherein said phosphonic acid-containing compound is a compound of any one of claims 1, 2, 117, 139, or 140.

Claim 240 (new): The method of claim 100 wherein said phosphonic acid-containing compound is a compound of any one of claims 1, 2, 117, 139, or 140.

Claim 241 (new): A pharmaceutical compositions comprising a pharmaceutically acceptable amount of a compound of any one of claims 1, 2, 117, 139, or 140.